REMARKS

Applicant's attorney wishes to thank Examiners Chunduru and Fredman for the courtesies extended during the interview of June 4, 2003.

Claims 13-14 currently appear in this application. The Office Action of December 16, 2002, has been carefully studied. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicants respectfully request favorable reconsideration, entry of the present amendment, and formal allowance of the claims.

The Invention

The present invention is directed to a method for detecting potential endocrine disruptors of which the endocrine-disrupting activity is unknown using a DNA array onto which many types of genes are immobilized, these genes being those the expression of which may be influenced by an endocrine disruptor.

The invention defined by new claim 13 is directed to a method for determining a signal transduction pathway that is influenced by an endocrine disrupting activity of a test substance. Support for this claim can be found in the specification as filed at page 10, line 23 to page 43, line 9. specifically, the method of the present invention can be used to detect the expression of genes that are influenced by endocrine disruptors (for example, a gene for a nuclear receptor in a cell and a number of genes involved in the downstream signal

transduction pathway, as described in the specification at page 43, liens 1-9).

Claim 14 is directed to a method for determining a substance that causes endocrine disruption in a manner similar to a known endocrine disruption. In claim 14, the genes on the DNA array comprise at least one gene for each of the respective groups (1) to (17) as recited in claim 14. These genes are described in the specification as filed at page 15, line 22 to page 17, line 3.

Claim 14 is supported by the specification as filed at page 44, line 14 to page 45, line 22.

Prior to the present invention, there existed only techniques for analyzing the relationship between the expression of one given gene and a test substance, or methods which involved using a DNA chip having an unspecified number of immobilized genes for analyzing the relationship between expression of the genes and a test sample. In the present invention, the genes in the DNA array comprise at least one gene for each of the respectively specified groups. This technique is neither disclosed nor suggested in the cited art.

Rejections under 35 U.S.C. 112

Claims 1-6 and 10-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject mater which applicant regards as the invention.

This rejection is respectfully traversed. Claims 1-12 have been replaced by newly submitted claims 13-15. New claims 13-15 do not include the phrase "potentially influenced."

Art Rejections

Claims 1, 3, and 5 are rejected under 35 U.S.C. 102(e) as being anticipated by Adams et al.

This rejection is respectfully traversed. New claims 13-16 recite that a **series** of genes are identified in which the expression levels are altered as a result of the exposure of the cell to the test substance. By identifying such a **series** of genes one can determine a signal transduction pathway that is influenced by an endocrine disrupting activity of a test substance, or a substance that causes endocrine disruption in a manner similar to an endocrine disruptor. The DNA array recited in claim 16 is used for such determination.

Adams discloses a method for determining if a substance is an endocrine disruptor, but, as stated in the specification as filed at page 2, beginning at the last paragraph, it has not yet been clearly demonstrated to date whether or nor the substances that are suspected to be endocrine disruptors will actually cause endocrine disruption, and, if they cause endocrine disruption, the mechanism through which these substances influence as well as the amount and the length of period of intake that might pose risk for animals has not been clearly demonstrated.

As noted in the specification at page 2, first

full paragraph, just because a substance binds to a hormone receptor is not sufficient evidence that the substance is indeed a hormone disruptor which may cause problems. For example, estradiol, diethylstilbestrol, isoflavone, and bisphenol-A all bind to the estrogen receptor. However, the EC_{50} values for these substances are different from each other. Thus, the conventional assay methods cannot determine the degree of endocrine disruption.

There is nothing in Adams that discloses or suggests using a series of genes to identify an endocrine disruptor or to identify the pathway by which this endocrine disruption occurs.

Claims 2, 4, 6, 7 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adams et al. in view of Kuiper et al. The Examiner states that Adams et al. teach a method for detecting a gene or substance that is influenced by an endocrine disruptor. The Examiner concedes that Adams et al. did not teach nuclear receptor gene as the gene influenced by the endocrine disruptor as phenol substances or compounds. Kuiper et al. are said to teach a method for interaction of estrogenic chemicals and phytoestrogens with estrogen receptor, wherein Kuiper et al. are said to disclose that the method comprises transient expression of estrogen receptor response element in response to the chemical compounds.

This rejection is respectfully traversed. There is nothing in Kuiper et al. that supplies the missing element of Adams et al., namely, that a **series** of genes in which the

expression levels are altered as a result of exposing the cells to the test substance.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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